

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

MAR 27 2000 3:26PM

BIOMEDICAL INFO SERV

NO. 3939

P. 55/65

*Sample
Copy*



JVIR

Journal of Vascular and Interventional Radiology

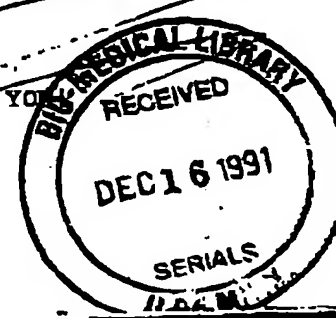
AUGUST 1991 • VOLUME 2 • NUMBER 3

~~PLEASE RETURN THIS SAMPLE~~

~~JOURNAL WITH YOUR JOURNAL~~

~~RECOMMENDATION.~~

THANK YOU



MAR. 27. 2000 3:33PM

BIOMEDICAL INFO SERV

NO. 3939

P. 56/65

(B) NOTICE: THIS MATERIAL MAY BE PROTECTED
BY COPYRIGHT LAW (TITLE 17 U.S. CODE)

Aortic Bifurcation Stenosis: Treatment with Intravascular Stents¹

Julio C. Palmaz, MD²
Carlos E. Encarnacion, MD
Oscar J. Garcia, MD
Richard A. Schwarz, MD²
Frank J. Rivera, MD
Jean Claude Labonde, MD
Sarsfield P. Dougherty, MD

Index terms: Aorta, grafts and prostheses, 89.461, 891.456 • Aorta, stenosis or obstruction, 991.721 • Arteries, grafts and prostheses, 89.461, 891.456, 894.456 • Arteries, iliac, 884.456

JVIR 1991; 2:319-323

Abbreviation: HATS = hypoplastic aortic arch syndrome

Balloon-expandable intravascular stents were employed to correct atherosclerotic stenosis of the aortic bifurcation. The devices were placed in the proximal iliac arteries with the cephalic end of the stents contacting in the midline. This arrangement provided an adequate lumen for the distal portion of the aortic wall and the proximal iliac arteries. Six of seven patients who received this form of treatment had hemodynamic and clinical improvement of their vascular insufficiency at an average follow-up of 1 year.

ALTHOUGH atherosclerotic disease has varied anatomic distributions and clinical manifestations, certain anatomic patterns have been identified (1). It is well known that atherosclerotic disease at the aortic bifurcation occurs frequently and does not commonly produce severe symptoms of lower extremity ischemia, such as skin ulcer or gangrene, unless femoropopliteal or distal arterial obstructions are present (2). However, this association is uncommon; the arteries distal to aortoiliac stenoses or occlusions usually have little or no involvement.

Because aortic bifurcation disease is often localized, it lends itself well to treatment by means of percutaneous therapy. A small series of patients with this problem were treated with balloon-expandable stents and were followed up clinically for a mean period of 1 year.

PATIENTS AND METHODS

Seven patients (four women and three men), with a mean age of 59 years (range, 58-70 years), were evaluated for symptoms of ischemia caused by atherosclerotic disease at the aortic bifurcation. Five patients had bilateral stenoses at the aortic bifurcation and proximal common iliac arteries, and two had unilateral

common iliac artery occlusion with contralateral common iliac stenosis. All patients had smoked an average of 1.5 packs of cigarettes per day for 36 years. Two patients had diabetes mellitus, and five had high blood pressure. Two were moderately obese, four had documented coronary artery disease, and one had evidence of cerebrovascular disease. Of three patients with a limb at risk, two had rest pain and one had nonhealing skin ulcers and toe gangrene. Three patients had severe intermittent claudication, and one had life-style-limiting claudication. The patient with life-style-limiting claudication had undergone percutaneous balloon angioplasty of the proximal iliac arteries, but his symptoms recurred 6 months after treatment. The mean ankle-brachial index in this group of patients was 0.65 ± 0.26 . Arteriograms showed narrowing of the distal aortic lumen and stenosis or occlusion of the proximal common iliac arteries in all patients. Six of the patients had normal femoropopliteal and distal vessels. One diabetic patient had bilateral severe disease of the tibioperoneal arteries.

The procedure was performed via a percutaneous bilateral femoral approach following indications, contraindications, and technique of an investigational device exception research protocol (3). After successful

¹ From the Section of Cardiovascular and Special Interventions, Department of Radiology, University of Texas Health Science Center, 7703 Floyd Curl Dr, San Antonio, TX 78294 (J.C.P., C.E.E., O.J.G., F.J.R., J.C.L., S.P.D.), and the Scripps Clinic, San Diego (R.A.S.). Received December 14, 1990; revision requested January 27, 1991; revision received March 21; accepted March 30. Address reprint requests to J.C.P.

² J.C.P. and R.A.S. have a financial relationship with corporations whose products or services are related to the subject matter of this article.

© SCVIR, 1991

MAR. 27. 2000 3:34PM

BIOMEDICAL INFO SERV

NO. 3939

P. 57/65

320 - Journal of Vascular and Interventional Radiology

August 1991

guide wire passage, the lesions were crossed with 5-F straight catheters within a vascular sheath for simultaneous aortic and distal iliac pressure recording and assessment of gradients before and after vasodilation. The mean transtentotic pressure gradient was $25.9 \text{ mm Hg} \pm 13.9$. After injection of contrast material, the angiographic catheters were exchanged for balloon angioplasty catheters to allow simultaneous dilation of the aortic bifurcation and proximal common iliac arteries (kissing balloons) according to a previously reported technique (4). After balloon angioplasty, pelvic angiograms and a new set of pressure recordings and gradients were obtained. Stents were placed if the pressure gradient was equal to or larger than 5 mm Hg after vasodilation or if the vessel diameter at the angioplasty site decreased by 30% or more of that achieved with balloon inflation.

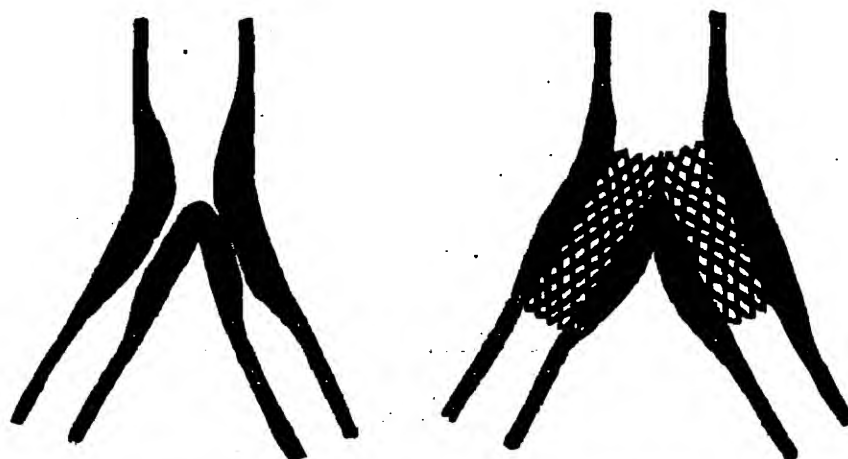


Figure 1. Schematic representation of atherosclerotic stenosis predominantly affecting the aortic bifurcation and origin of the iliac arteries. Bilateral stents placed with the cephalic ends contacting in the midline provide support for the most distal portion of the aortic wall.

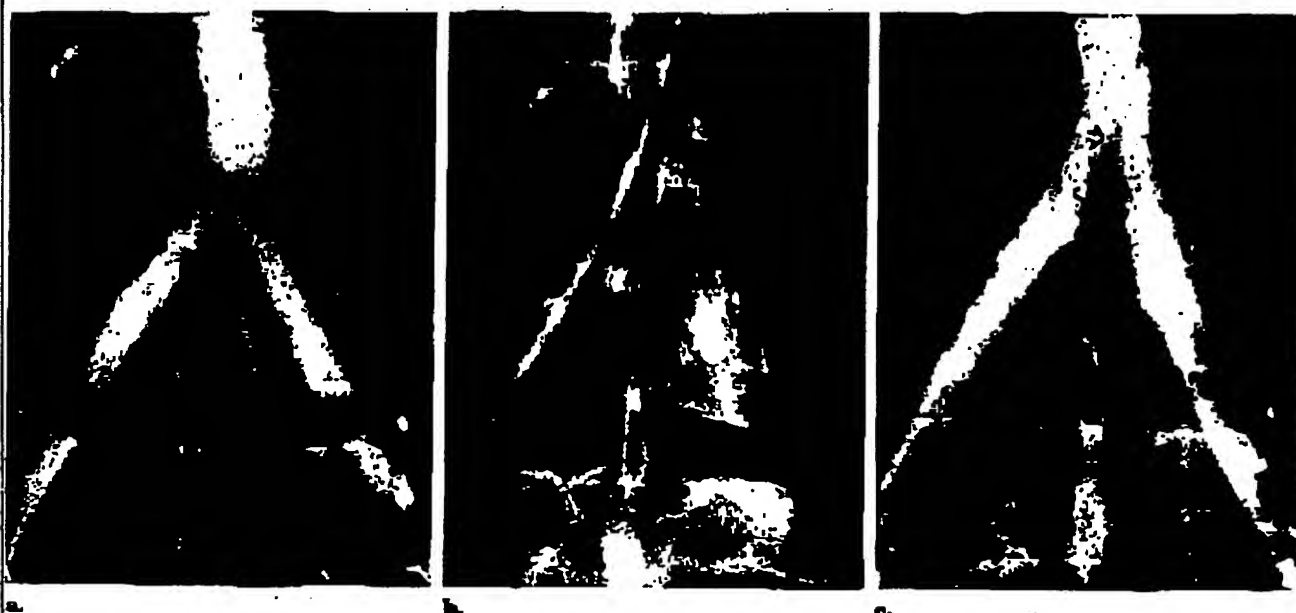


Figure 2. Abdominal aortic bifurcation of a 54-year-old woman with intermittent claudication. (a) Distal aortic diameter measured 11 mm after correction for magnification. Intraluminal mean pressure gradients were 18 mm Hg across the right common iliac artery stenosis and 29 mm Hg across the left. (b) After placement of single iliac stents bilaterally, the pressure gradients were reduced to 4 mm Hg on the left and zero on the right. (c) Injection of contrast material demonstrates restoration of patency at the bifurcation. An opaque line indicates the midline overlap of the stents (arrow).

MAR. 27. 2000 3:34PM

BIOMEDICAL INFO SERV

NO. 3939 P. 58/65

Palmas et al - 321

Volume 2 Number 3

Immediately prior to stent placement, 30-cm-long, 10-F introducer sheaths were introduced into each femoral artery with the tips located above the aortic bifurcation. One stent-balloon assembly was positioned at the target level in one side while an angioplasty balloon was placed at the same level through the opposite sheath. After partial withdrawal of the sheaths, manual injections of contrast medium were recorded with a digital subtraction technique and were used for precise positioning. The balloon without a stent was inflated first with diluted contrast medium. The stent was expanded by inflating the corresponding balloon with saline. This allowed fluoroscopic control of the stent expansion as the balloon was inflated. The opposing balloon was then deflated and exchanged for a stent-balloon assembly following repositioning of the sheath's tip above the aortic

bifurcation. Prior to expansion of the second stent, the balloon that deployed the first stent was reinflated. Both stents were deployed with their proximal ends contacting in the midline, 3-5 mm above the aortic bifurcation. This was done to stent the distal aortic wall as well as the proximal iliac arteries (Fig 1).

RESULTS

Four patients received one stent on each side (Figs 2, 3), one patient required two stents in tandem in one iliac artery and a single stent in the opposite one, and two patients received two stents in tandem in each side. Midline contact of opposing stents produced a prosthetic ridge cephalad to the aortic bifurcation that was visible on the angiogram obtained after stent placement in all seven patients (Fig 2c). The average

transluminal mean pressure gradient between the proximal aorta and the distal iliac arteries of $25.9 \text{ mm Hg} \pm 13$ was reduced to $1.8 \text{ mm Hg} \pm 2.8$ after the procedure.

Prior to hospital discharge, six patients were free of peripheral vascular symptoms. An insulin-dependent diabetic patient with toe gangrene and a persistent nonhealing foot ulcer underwent subsequent femoral and tibial artery balloon angioplasty in an attempt to forestall amputation. Two weeks later, she underwent toe amputation; this failed to heal, and a transmetatarsal amputation was required 6 weeks later. This also failed to heal, and 3 months after stent placement, she underwent a below-the-knee amputation and was discharged in good condition. At the latest mean follow-up of 9 months (range, 3-13 months), all patients were asymptomatic. Their ankle-brachial systolic pressure index in-

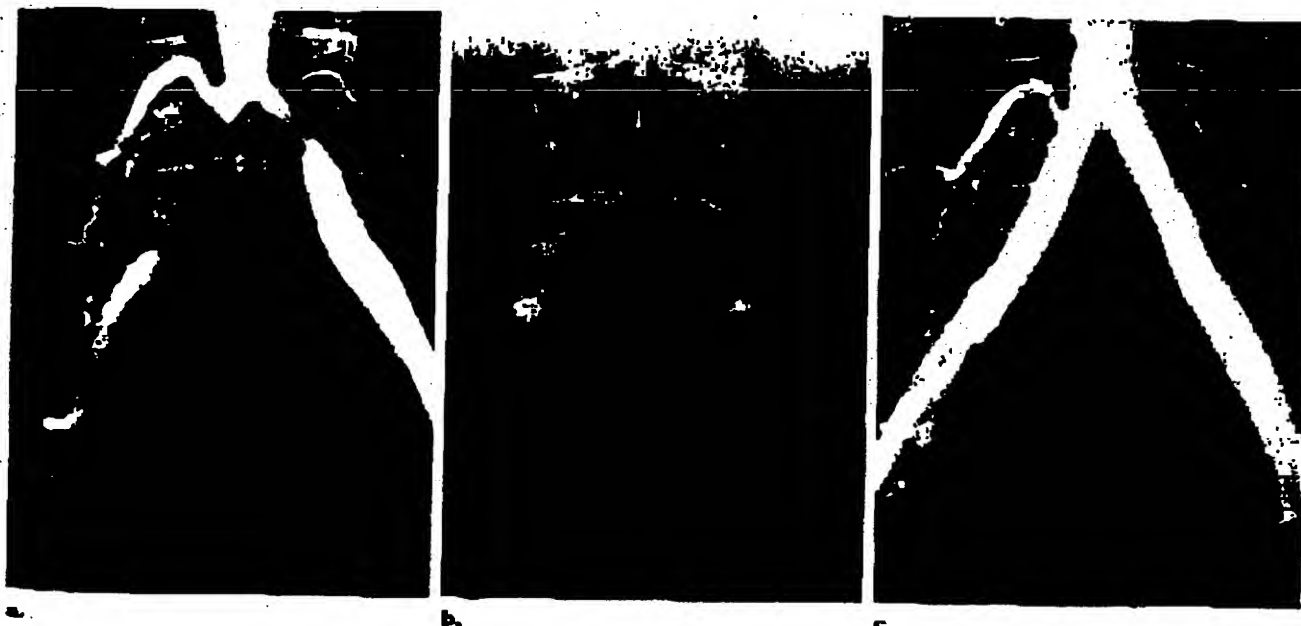


Figure 3. Abdominal aortic bifurcation of a 54-year-old woman with bilateral, severe buttock and lower extremity intermittent claudication. (a) Distal aortic diameter measured 9 mm after correction for magnification. After bilateral common iliac artery angioplasty with 8-mm balloons, there were residual pressure gradients of 10 mm Hg in the right iliac artery and 8 mm Hg in the left iliac artery. (b) After placement of kissing stents, no pressure gradient was detected. (c) Aortogram demonstrates restoration of the lumen of the aortodilator junction. A linear dissection is present in the distal right common iliac and proximal external iliac arteries. Because of the absence of a significant gradient, no further therapy was undertaken.

MAR. 27. 2000 3:35PM

BIOMEDICAL INFO SERV

NO. 3939 P. 59/65

322 - Journal of Vascular and Interventional Radiology

August 1991

creased from 0.65 ± 0.26 to 0.84 ± 0.28 at the time of hospital discharge and was 0.9 ± 0.24 at the latest follow-up. All patients were strongly encouraged to quit smoking. Despite counseling, one patient continued smoking after the procedure.

One complication occurred: One patient experienced thrombosis of the common femoral artery at the puncture site a few hours after withdrawal of the sheath. The obstruction was successfully managed with intra-arterial infusion of urokinase from the contralateral femoral approach without significant bleeding from the previous puncture site.

DISCUSSION

According to Watt (2), atherosclerotic stenosis predominantly affecting the distal abdominal aorta and the origin of the iliac arteries is more common than isolated disease of the common and external iliac arteries. The symptoms of ischemia produced by this disease usually develop during the 5th decade of life, 5–15 years earlier than in the majority of patients with lower extremity arterial disease (5,6). Because of its possible relationship to congenital hypoplasia of the distal aorta, aortic bifurcation stenosis, predominantly seen in female smokers, has been termed hypoplasia aortofemoral syndrome (HAIS) (7). The association of congenital aortic hypoplasia and lower extremity ischemia, first described by John Baptist Morgagni in 1733 (8), has been reported by several other authors (9–12). Embryonal overfusion of the paired primitive aortae resulting in a small aortic diameter and an excessively tapered distal aorta was suggested by Arnet and Louw (13) as possibly being related to HAIS. Other possible causes are the rubella syndrome (14), Takayasu arteritis (15), and ionizing radiation (16).

The role of tobacco in this disease is not clear. It may potentiate the atherogenic influence of the hemodynamic stress caused by the abnormally tapered aorta. The aortic bifur-

cation constitutes the first obstacle to the progression of the blood flow from the aortic valve, causing pulse reflections that may originate standing pressure waves. An ideal ratio of the cross-sectional area of the iliac arteries to the aorta of 1.15, causing the least amount of pulse-wave reflections, is present in humans at birth. Unfortunately, this ratio progressively decreases with age, causing increased stress on the aortic wall (17).

Compared with the aortae of other animal species, the human abdominal aorta has a larger proportion of medial lamellar units without vasa vasorum that depend on transmural diffusion of nutrients and oxygen. Also, the human abdominal aortic wall supports a higher stress per lamellar unit compared with the thoracic aorta or with other mammalian avascular aortic media (18).

The reason for the female predominance in this disease remains unexplained. The association of aortic bifurcation stenosis, a small distal aorta, and cigarette smoking is also present in men but occurs less frequently (19). Just as in women with HAIS, bifurcation disease in men tends to occur at an earlier age than predominantly distal arterial disease (19).

Reconstructive surgery has been an effective treatment for distal aortic disease (5,7,10). De Laurentis et al (7) reviewed a series of 18 patients with HAIS who were treated with Dacron bypass procedures. These authors recognized the increased risk of graft failure in these patients and emphasized the need for long end-to-side anastomoses because of the small diameter of the arteries involved. Jernigan et al (6) obtained better patency rates in patients treated with thromboendarterectomy and onlay vein patching of the aortic bifurcation than in those who received bypass grafts. Burke et al (10) found that the cumulative patency of Dacron aortofemoral bypass in patients with HAIS was only 52% at 4 years and advocated the use of polytetrafluoroethylene and distal profundaplasty to improve results. The overall patency rates for these three series of 70 HAIS patients treated with bypass techniques averaged 76% at an average follow-up of 5.1 years.

The use of balloon angioplasty techniques has been reported in patients with aortic bifurcation disease. The review by Becker et al (20) of balloon angioplasty of the distal aorta and the aortic bifurcation indicated an average technical success rate of 92% and clinical success rate of 83%

Comparison between Balloon Angioplasty and Stent Placement in Patients with Aortic Bifurcation Disease

Variable	Balloon Angioplasty (n = 52)	Stent Placement (n = 7)
Technical success (%)	92	100
Clinical success (%)	83	86
Residual gradient (mm Hg)	6	1.3
Preprocedural ABI	0.59	0.65
Postprocedural ABI	0.89	0.90
Mean follow-up (mo)	12	9
Female patients (%)	75	57
Age (y)	54	59
Cigarette smoking (%)	96	100
Diabetes mellitus (%)	12	29
High blood pressure (%)	29	71
Limbs at risk of amputation (%)	9	42
Complications (%)	16	15

Source.—Data are from references 4, 21, and 22.

Note.—ABI = ankle-brachial index.

MAR 27 2000 3:36PM

BIOMEDICAL INFO SERV

NO. 3939 P. 60/65

Palmas et al • 323

Volume 3 Number 3

at an average follow-up of 12 months. The technical and clinical success rates in our small series of patients treated with stents is similar (100% and 88%, respectively, Table). A greater hemodynamic improvement was obtained in our patients, as indicated by a residual mean pressure gradient of 1.8 mm Hg compared with 6 mm Hg in previously reported balloon angioplasty series (4,21,22). This may not be of significance since the ankle-brachial systolic pressure index obtained after the procedure was almost the same in our patients as in the study groups reported in the literature (4,21,22). However, a comparatively greater benefit may be present in our patients considering the higher proportion of limbs at risk of amputation (42% vs 8%) and higher prevalence of diabetes mellitus (29% vs 12%).

The postprocedural femoral artery thrombosis, the single significant complication in our series, reflects the risk of thrombosis imposed by the small-diameter peripheral arteries in these patients. This underlines the need for adequate heparinization and short procedure time.

In the single patient who eventually underwent below-the-knee amputation, the stump may not have healed without the improved inflow afforded by the procedure; without it, greater tissue loss could have resulted.

The lack of direct contact between stent and aortic wall at the point where opposing stents meet in the midline raises questions about possible lack of intimalization of the metal surface and potential hemolysis and/or thrombogenesis. Our patients did not show evidence of either complication. Metal is directly exposed to high-velocity flow in patients with

prosthetic aortic valves without causing significant hemolysis.

Direct comparisons between the results of surgery and stent placement in the treatment of HAIAS are not possible because of the small number of patients and short follow-up of the patients in the stent series. However, the obvious benefits of lower cost and shorter hospitalization time associated with stent placement make it an attractive alternative deserving further study.

Acknowledgment: The authors thank Cono Farias for his photographic assistance.

References

1. DeBakey ME, Lawrie GM, Glaeser DH. Patterns of atherosclerosis and their surgical significance. *Ann Surg* 1968; 201:115-131.
2. Watt JK. Pattern of aorto-iliac occlusion. *Br Med J* 1966; 3:979-981.
3. Palmas JC, Garcia OJ, Schatz RA, et al. Placement of balloon-expandable intraluminal stents in iliac arteries: first 171 procedures. *Radiology* 1990; 174:969-976.
4. Tegtmeyer CJ, Kellum CD, Kron IL, Mentzer RM. Percutaneous transluminal angioplasty in the region of the aortic bifurcation. *Radiology* 1985; 157:661-665.
5. Gallino A, Mahler P, Probst P, Naehbur B. Percutaneous transluminal angioplasty of the arteries of the lower limbs: a 5-year follow-up. *Circulation* 1984; 70:619-623.
6. Jernigan WR, Fallat ME, Hatfield DR. Hypoplastic aortoliliac syndrome; an entity peculiar to women. *Surgery* 1983; 94:752-757.
7. De Laurentis DA, Friedman P, Wolferth OC, Wilson A, Naida D. Atherosclerosis and the hypoplastic aortoliliac system. *Surgery* 1978; 83: 27-37.
8. Morgagni JB, Alexander B, trans. The seats and causes of diseases investigated by anatomy. Vol 2. London: 1769; letter 30, article 13.
9. Ben-Shoshan M, Rossi NP, Korns ME. Coarctation of the abdominal aorta. *Arch Pathol* 1973; 25:221-225.
10. Burke J. Congenital narrowness of the aortic system. *N Y State J Med* 1902; 2:283-297.
11. Maycock d'A W. Congenital stenosis of the abdominal aorta. *Am Heart J* 1937; 15:633-646.
12. Ritchie HD, Douglas DM. Atresia of the abdominal aorta. *Br Med J* 1956; 1:144-145.
13. Arnot RS, Louw JH. The anatomy of the posterior wall of the abdominal aorta. *S Afr Med J* 1973; 47:899-902.
14. Sissal B, Klyman G, Emmanouilides JC. Hypoplasia of the abdominal aorta associated with rubella syndrome. *Am J Dis Child* 1970; 120: 475-479.
15. Lande A. Takayasu's arteritis and congenital coarctation of the descending thoracic and abdominal aorta; a critical review. *AJR* 1978; 127:227-233.
16. Colquhoun J. Hypoplasia of the abdominal aorta following therapeutic irradiation in infancy. *Radiology* 1988; 68:454-456.
17. Gosling RG, Newman DL, Bowden NLR, Twinn RW. The area ratio of normal aortic junctions. *Br J Radiol* 1971; 44:850-853.
18. Wolinsky H, Glagov S. Comparison of abdominal and thoracic aortic medial structure in mammals. *Circ Res* 1969; 25:677-686.
19. Palmas JC, Carson SN, Hunter G, Weinshelbaum A. Male hypoplastic infrarenal aorta and premature atherosclerosis. *Surgery* 1983; 94:91-94.
20. Becker GJ, Katzen BT, Dake MD. Noncoronary angioplasty. *Radiology* 1989; 170:921-940.
21. Heery D, Bookstein J, Daniels E, Wormath M, Horn J, Rowley W. Transluminal angioplasty of the abdominal aorta. *Radiology* 1983; 148: 81-83.
22. Charlebois N, Saint-George G, Hndon G. Percutaneous transluminal angioplasty of the lower abdominal aorta. *AJR* 1986; 148:369-371.